

WEST

Generate Collection

L10: Entry 5 of 6

File: DWPI

May 1, 1998

DERWENT-ACC-NO: 1997-145355

DERWENT-WEEK: 200007

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Use of new and known 1-alkyl-1,4-dihydro-4-oxo-N-subst
naphthyridine-3-carboxamide derivs - for treating conditions modulated by
phosphodiesterase IV or tumour necrosis factor

INVENTOR: BAXTER, A D; BEASLEY, S C; BUCKLEY, G M; DYKE, H J; HAUGHAN, A F;
KENDALL, H J; MANALLACK, D T; MAXEY, R J; MONTANA, J G; RUNCIE, K A; HAUGHAN,
F A

PATENT-ASSIGNEE:

ASSIGNEE

CODE

CHIROSCIENCE LTD

CHIRN

DARWIN DISCOVERY LTD

DARWN

PRIORITY-DATA: 1996GB-0011898 (June 7, 1996), 1995GB-0015812 (August 2, 1995),
1995GB-0023679 (November 20, 1995), 1996GB-0005865 (March 20, 1996)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
MX 9800921 A1	May 1, 1998	N/A	000	A61K031/435
WO 9704775 A1	February 13, 1997	E	033	A61K031/435
AU 9666266 A	February 26, 1997	N/A	000	N/A
ZA 9606600 A	October 29, 1997	N/A	031	A61K000/00
EP 841927 A1	May 20, 1998	E	000	N/A
US 5753666 A	May 19, 1998	N/A	000	A01N043/54
AU 695132 B	August 6, 1998	N/A	000	N/A
JP 11510156 W	September 7, 1999	N/A	037	A61K031/44

DESIGNATED-STATES: AL AM AU AZ BB BG BR BY CA CN CU CZ EE GB GE HU IL IS JP KE KG
KP KR KZ LK LR LS LT LV MD MG MK MN MW MX NO NZ PL RO RU SD SG SI SK TJ TM TR TT
UA UG UZ VN AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE
SZ UG AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE

CITED-DOCUMENTS: 6.Jnl.Ref; JP 2124871 ; US 3524858 ; US 4621088 ; US 4786644

APPLICATION-DATA:

Stoke
HIV
Alvin Vinal - influenza
flap

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
MX 9800921A1	February 2, 1998	1998MX-0000921	N/A
WO 9704775A1	July 31, 1996	1996WO-GB01866	N/A
AU 9666266A	July 31, 1996	1996AU-0066266	N/A
AU 9666266A		WO 9704775	Based on
ZA 9606600A	August 2, 1996	1996ZA-0006600	N/A
EP 841927A1	July 31, 1996	1996EP-0925909	N/A
EP 841927A1	July 31, 1996	1996WO-GB01866	N/A
EP 841927A1		WO 9704775	Based on
US 5753666A	August 2, 1996	1996US-0691339	N/A
AU 695132B	July 31, 1996	1996AU-0066266	N/A
AU 695132B		AU 9666266	Previous Publ.
AU 695132B		WO 9704775	Based on
JP 11510156W	July 31, 1996	1996WO-GB01866	N/A
JP 11510156W	July 31, 1996	1997JP-0507375	N/A
JP 11510156W		WO 9704775	Based on

INT-CL (IPC): A01N 43/54; A61K 0/00; A61K 31/00; A61K 31/435; A61K 31/44; A61K 31/47; A61K 31/505; C07D 471/00; C07D 471/04

RELATED-ACC-NO: 1997-153912

ABSTRACTED-PUB-NO: US 5753666A
BASIC-ABSTRACT:

The use of 1-alkyl-4-(thi)oxo-naphthyridine-3-carboxamide derivs. and -pyrido(2,3-d)pyrimidine analogues of formula (I), their salts, solvates and/or hydrates in the mfr. of a medicament for treating disease states modulated by phosphodiesterase IV (PDE-IV) or tumour necrosis factor (TNF) inhibition, is new. R1 = 1-6C alkyl, 1-6C alkylcycloalkyl, 1-6C alkyl-heterocyclo, 1-6C alkylaryl or 1-6C alkylheteroaryl all opt. substd. by 1 or more T, 1-6C alkyl or SO₂NR₁₁R₁₂; T = halo, 1-6C alkoxy, OH, CN, COOH (or its 1-6C alkyl ester or 1-6C alkylamide) or NR₉R₁₀; R₃ = phenyl, pyridyl, thienyl, furyl, pyrazinyl, pyridazinyl, pyrimidinyl or 3-10C cycloalkyl all opt. fused to a carbocyclic or heterocyclic ring and both rings opt. substd. by T, 1-6C alkyl, 1-6C haloalkyl, SO₂NR₁₁R₁₂, aryl, heteroaryl, cycloalkyl or heterocyclo; Y = O or S; X = CR₅ or N; Q = CR₇ or N; R₄-R₇ = H, T, or 1-6C alkyl (opt. substd. by T or SO₂NR₁₁R₁₂); or two adjacent R₄-R₇ gps. complete a 5- or 6-membered ring opt. contg. 1 or 2 heteroatoms; R₉, R₁₀ = H, 1-6C alkyl, aryl, heteroaryl, COCF₃, SO₂CF₃, cycloalkyl, 1-6C C alkylcarbonyl, aroyl, 1-6C alkoxy carbonyl, arylsulphonyl or 1-6C alkylsulphonyl; or NR₉R₁₀ = 5- or 6-membered ring e.g. pyrrolidino, piperidino, morpholino or piperazino; R₁₁, R₁₂ = H, 1-6C alkyl or cycloalkyl; n = 0-3; provided that (1) at least 1 of X and Q = N; and (2) when R₃ = substd. cyclohexyl and n = 1, the substituent is not COOH or its ester. Also claimed are cpds. (I) provided that when R₃ is attached to (CH₂)_n at an aromatic atom, n = 1-3.

USE - (I) are useful for treating disease states associated with proteins which mediate cellular activity. (I) are partic. useful for treating disease states associated with a function of PDE IV, eosinophil accumulation or function or TNF (esp. inflammatory or autoimmune disease) such as asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, inflammation or allergic responses in the eye, eosinophilic granuloma, psoriasis, rheumatoid arthritis, gouty arthritis, arthritic conditions, ulcerative colitis, Crohn's disease, adult respiratory distress syndrome, diabetes insipidus, keratosis, atopic eczema, atopic dermatitis, cerebral senility, multi-infarct dementia, senile dementia, memory impairment associated with Parkinson's disease, depression, cardiac arrest, stroke, intermittent claudication, joint inflammation, rheumatoid spondylitis, osteoarthritis, sepsis, septic shock, endotoxic shock, Gram negative sepsis, toxic shock syndrome, cerebral malaria, chronic pulmonary inflammatory disease, pulmonary sarcoidosis, bone resorption disease, reperfusion injury, graft vs. host reaction, allograft rejection, malaria, myalgia, HIV, AIDS, ARC, cachexia, pyresis, systemic lupus

erythematosus, multiple sclerosis, type 1 diabetes mellitus, Bechet's disease, anaphylactoid purpura nephritis, chronic glomerulonephritis, inflammatory bowel disease, leukaemia or tardive dyskinesia (all claimed).

(I) are also useful as gastro-protectants and agents for treating yeast or fungal infections (claimed) (e.g. fungal meningitis).

(I) can also be used to treat viruses sensitive to TNF inhibition e.g. HIV-1, -2 or -3, cytomegalovirus, influenza, adenovirus, Herpes viruses (e.g. Herpes zoster and Herpes simplex), feline immunodeficiency virus and other animal retroviruses such as equine infectious anaemia, caprine arthritis, visna virus, maedi virus and other lentiviruses.

The excluded cpds. are disclosed in US4621088.

Dose is 0.001-20 mg/kg/day. Admin. is oral, rectal, topical, parenteral or via the respiratory tract.

ABSTRACTED-PUB-NO:

WO 9704775A

EQUIVALENT-ABSTRACTS:

The use of 1-alkyl-4-(thi)oxo-naphthyridine-3-carboxamide derivs. and -pyrido(2,3-d)pyrimidine analogues of formula (I), their salts, solvates and/or hydrates in the mfr. of a medicament for treating disease states modulated by phosphodiesterase IV (PDE IV) or tumour necrosis factor (TNF) inhibition is new. R1 = 1-6C alkyl, 1-6C alkylcycloalkyl, 1-6C alkyl-heterocyclo, 1-6C alkylaryl or 1-6C alkylheteroaryl all opt. substd. by 1 or more T, 1-6C alkyl or SO₂NR₁₁R₁₂; T = halo, 1-6C alkoxy, OH, CN, COOH (or its 1-6C alkyl ester or 1-6C alkylamide) or NR₉R₁₀; R3 = phenyl, pyridyl, thienyl, furyl, pyrazinyl, pyridazinyl, pyrimidinyl or 3-10C cycloalkyl all opt. fused to a carbocyclic or heterocyclic ring and both rings opt. substd. by T, 1-6C alkyl, 1-6C haloalkyl, SO₂NR₁₁R₁₂, aryl, heteroaryl, cycloalkyl or heterocyclo; Y = O or S; X = CR₅ or N; Q = CR₇ or N; R₄-R₇ = H, T, or 1-6C alkyl (opt. substd. by T or SO₂NR₁₁R₁₂); or two adjacent R₄-R₇ gps. complete a 5- or 6-membered ring opt. contg. 1 or 2 heteroatoms; R₉, R₁₀ = H, 1-6C alkyl, aryl, heteroaryl, COCF₃, SO₂CF₃, cycloalkyl, 1-6C C alkylcarbonyl, aroyl, 1-6C alkoxy carbonyl, arylsulphonyl or 1-6C alkylsulphonyl; or NR₉R₁₀ = 5- or 6-membered ring e.g. pyrrolidino, piperidino, morpholino or piperazino; R₁₁, R₁₂ = H, 1-6C alkyl or cycloalkyl; n = 0-3; provided that (1) at least 1 of X and Q = N; and (2) when R₃ = substd. cyclohexyl and n = 1, the substituent is not COOH or its ester. Also claimed are cpds. (I) provided that when R₃ is attached to (CH₂)_n at an aromatic atom, n = 1-3.

USE - (I) are useful for treating disease states associated with proteins which mediate cellular activity. (I) are partic. useful for treating disease states associated with a function of PDE IV, eosinophil accumulation or function or TNF (esp. inflammatory or autoimmune disease) such as asthma, chronic bronchitis, atopic dermatitis, urticaria, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, inflammation or allergic responses in the eye, eosinophilic granuloma, psoriasis, rheumatoid arthritis, gouty arthritis, arthritic conditions, ulcerative colitis, Crohn's disease, adult respiratory distress syndrome, diabetes insipidus, keratosis, atopic eczema, atopic dermatitis, cerebral senility, multi-infarct dementia, senile dementia, memory impairment associated with Parkinson's disease, depression, cardiac arrest, stroke, intermittent claudication, joint inflammation, rheumatoid spondylitis, osteoarthritis, sepsis, septic shock, endotoxic shock, Gram negative sepsis, toxic shock syndrome, cerebral malaria, chronic pulmonary inflammatory disease, pulmonary sarcoidosis, bone resorption disease, reperfusion injury, graft vs. host reaction, allograft rejection, malaria, myalgia, HIV, AIDS, ARC, cachexia, pyresis, systemic lupus erythematosus, multiple sclerosis, type 1 diabetes mellitus, Bechet's disease, anaphylactoid purpura nephritis, chronic glomerulonephritis, inflammatory bowel disease, leukaemia or tardive dyskinesia (all claimed).

(I) are also useful as gastro-protectants and agents for treating yeast or fungal infections (claimed) (e.g. fungal meningitis).

(I) can also be used to treat viruses sensitive to TNF inhibition e.g. HIV-1, -2 or -3, cytomegalovirus, influenza, adenovirus, Herpes viruses (e.g. Herpes zoster and Herpes simplex), feline immunodeficiency virus and other animal retroviruses

such as equine infectious anaemia, caprine arthritis, visna virus, maedi virus and other lentiviruses.

The excluded cpds. are disclosed in US4621088.

Dose is 0.001-20 mg/kg/day. Admin. is oral, rectal, topical, parenteral or via the respiratory tract.

TITLE-TERMS: NEW ALKYL DI HYDRO OXO N SUBSTITUTE NAPHTHYRIDINE CARBOXAMIDE
DERIVATIVE TREAT CONDITION MODULATE PHOSPHODIESTERASE IV TUMOUR NECROSIS FACTOR

ADDL-INDEXING-TERMS:
PYRROLO PYRIMIDINE

DERWENT-CLASS: B02 C02

CPI-CODES: B06-D02; C06-D02; B06-D06; C06-D06; B14-C03; C14-C03; B14-C09B;
C14-C09B; B14-G02A; C14-G02A; B14-G02D; C14-G02D; B14-K01; C14-K01; B14-N17C;
C14-N17C; B14-S04; C14-S04;

CHEMICAL-CODES:

Chemical Indexing M2 *01*

Fragmentation Code

C316 D010 D011 D012 D013 D014 D019 D020 D021 D022
D023 D024 D025 D040 D622 D770 D850 F010 F019 F020
F021 F029 G001 G002 G003 G010 G011 G012 G013 G019
G020 G021 G022 G029 G040 G050 G100 G111 G221 G299
G553 G563 H1 H103 H121 H122 H123 H141 H161 H181
H2 H201 H401 H402 H403 H404 H441 H442 H443 H444
H481 H482 H483 H484 H521 H522 H523 H541 H542 H543
H581 H582 H583 H584 H600 H608 H609 H621 H622 H623
H641 H642 H643 H681 H682 H683 H689 J0 J011 J012
J013 J014 J111 J112 J113 J131 J132 J133 J171 J172
J173 J211 J212 J231 J232 J271 J272 J273 J3 J311
J5 J521 J592 K353 K399 L142 L143 L145 L199 L910
L921 L922 L930 L941 L943 L999 M126 M136 M210 M211
M212 M213 M214 M215 M216 M220 M221 M222 M223 M224
M225 M226 M231 M232 M233 M240 M272 M273 M281 M282
M283 M311 M312 M313 M314 M315 M316 M320 M321 M322
M323 M331 M332 M333 M334 M340 M342 M343 M344 M353
M372 M373 M391 M392 M393 M412 M511 M512 M520 M521
M522 M530 M531 M532 M540 M541 M542 M630 M640 M650
M781 M800 M903 M904 P420 P421 P423 P433 P444 P446
P522 P616 P738 P816 P820 P922 P924 P943 V813

Ring Index

01605 01681 01683

Markush Compounds

199713-40701-U

SECONDARY-ACC-NO:

CPI Secondary Accession Numbers: C1997-046367

=> d 18 ibib kwic 1-

·YOU HAVE REQUESTED DATA FROM 16 ANSWERS - CONTINUE? Y/(N):y

L8 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:713343 CAPLUS

DOCUMENT NUMBER: 135:272894

TITLE: Preparation of .beta.-amino acid derivatives as **inhibitors** of matrix metalloproteases and **TNF**-.alpha.

INVENTOR(S): Duan, Jingwu; King, Bryan W.; Decicco, Carl; Maduskuie, Thomas P., Jr.; Voss, Matthew E.

PATENT ASSIGNEE(S): Dupont Pharmaceuticals Company, USA

SOURCE: PCT Int. Appl., 483 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070734	A2	20010927	WO 2001-US8336	20010315
W:	AT, AU, BR, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, HU, IL, IN, JP, KR, LT, LU, LV, NZ, PL, PT, RO, SE, SG, SI, SK, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR			

PRIORITY APPLN. INFO.:
US 2000-190183 P 20000317
US 2000-235467 P 20000926
US 2000-252062 P 20001120

OTHER SOURCE(S): MARPAT 135:272894

TI Preparation of .beta.-amino acid derivatives as **inhibitors** of matrix metalloproteases and **TNF**-.alpha.

AB Novel .beta.-amino acid derivs. A-CR3R4aCR2R4NR1CO-X-Z-Ua-Xa-Ya-Za [A = CO2H, SH, CH2SH, S(O)Ra:NH (Ra = H, alkyl), P(O)(OH)2, etc.; X, Xa is absent or alkylene, alkenylene or alkynylene; Z is absent or substituted C3-13 carbocycle or 5-14 membered heterocycle; Ua is absent or O, NRal [Ral = H, (un)substituted alkyl, alkenyl or alkynyl; Ra and Ral may form a ring], CO, CO2, O2C, CONRal, S(O)p (p = 0-2), etc.; Ya is absent or O, NRal, S(O)p or CO; Za is H, substituted C3-13 carbocycle or 5-14 membered heterocycle; R1 is H, alkyl, Ph, benzyl; R2 is Q (Q is H, substituted carbocycle or heterocycle), alkylene-Q, (CRaRal)rlO(CRaRal)r-Q (r, rl = 0-4), (CRaRal)rlNRA(CRaRal)r-Q, etc.; R3 = Q1 (Q1 is any group given for Q), alkylene-Q1, (CRaRal)rlO(CRaRal)r-Q1, (CRaRal)rlNRA(CRaRal)r-Q1, etc.; R4, R4a = H, substituted alkyl, alkenyl or alkynyl; alternatively R1 and R2, R1 and R3, R3 and R4a may form rings (with provisos)] or a stereoisomer or pharmaceutically acceptable salt were prepd. as metalloprotease and **TNF**-.alpha. **inhibitors**. Thus, N-hydroxy-1-[[4-[(2-methyl-4-quinolinyl)methoxy]phenyl]acetyl]-3-azetidinecarboxamide was prepd. by a multistep procedure involving reactions of Me 4-hydroxyphenylacetate, 2-methyl-4-quinolinylmethanol, and 3-azetidinecarboxylic acid Me ester.

ST amino acid beta prepn **inhibitor** metalloprotease **TNF**; heterocyclyl beta amino acid prepn **inhibitor** metalloprotease **TNF**; cycloalkyl beta amino acid prepn **inhibitor** metalloprotease **TNF**

L8 ANSWER 4 OF 16 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001394010 EMBASE

TITLE: Involvement of protein kinase C in TNF.alpha. regulation of trabecular matrix metalloproteinases and TIMPs.

AUTHOR: Alexander J.P.; Acott T.S.

CORPORATE SOURCE: T.S. Acott, Casey Eye Institute (CERES), Oregon Health Sciences University, 3375 SW Terwilliger, Portland, OR 97201, United States. acott@ohsu.edu

SOURCE: Investigative Ophthalmology and Visual Science, (2001) 42/12 (2831-2838).